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MATHEMATICAL MODELING OF THE APPEARANCE OF MULTIPLE WAVES IN THE SARS-COV-2 CORONAVIRUS

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ABSTRACT

In this paper an analysis is made of the characteristics that the infection process by means of the SARS-CoV-2 coronavirus must present so that multiple waves can appear. A model is made that simulates this process according to the sign of the preceding numerical value of the infected population. When the sign is different from zero, conclusions are reached regarding the behavior of infected, recovered and susceptible populations, but when this sign is zero, the system that models the process is simplified, and applying the qualitative theory of differential equations conclusions are reached regarding the behavior of the process. At the end, graphs are made corresponding to concrete examples that corroborate the results obtained from the theoretical point of view.

KEYWORDS: Mathematical Model, epidemic, disease, transmission.

1. INTRODUCTION

The disease that has most affected humanity in recent years has been COVID-19. It is said that the cases of maximum risk are adults of the third age and especially those who suffer from some chronic disease; however, practice has shown that there is no one safe from this disease, and it can have a slow evolution or act swiftly.

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Due to these great effects that COVID-19 produces in the world, multiple results have been published both from the point of view of the biochemical characteristics, its treatment, and from the mathematics, which allows making predictions about the future behavior of the pandemic (Ramirez-Torres, et al., 2021), (Iborra, et al., 2020), (Reno, et al., 2020), (Ruiz, et al., 2020), (Zhao & Chen, 2020).

COVID-19 is a respiratory disease that has claimed many lives in the world, it is reported that to date it is present in 220 countries, with a total of 160 121 867 infections, 137 840 872 recovered and 3 325 621 deaths (Worldometer, 2021). There are many ideas on how to combat this disease, but the method that most researchers agree with is the method of isolating the infected to avoid possible transmission to other people (Montero, 2020).

One of the treatments that has already given results is interferon alpha-2b, in addition to others already tested in the treatment of other diseases such as AIDS, hepatitis, among others. Interferon alpha-2b, was developed by the Cuban Genetic Engineering and Biotechnology Center and has already been used in different parts of the world with highly reliable results (Pereda, et al., 2020), (Zhou, 2020).

Currently in Cuba, they are working with five vaccine candidates against COVID-19, which are passing through different phases of the clinical trial, Soberana 02 and Abdala that are passing through the third phase of the trial, Soberana 01, Soberana Plus and Mambisa that are passing through the second phase of the trial (Armas, 2020), (Infomed, 2021). In the particular case of the candidate, Mambisa explores the intranasal route, while the remaining candidates are intramuscularly (Infomed, 2021), particularly Soberana Plus is studied in convalescent patients.

The qualitative study of these models is very important, as this allows us to draw conclusions regarding the future situation of this process; allowing to determine necessary and sufficient conditions under which a possible complication could or could not be prevented. In (Ruiz, et al., 2018) different real life problems are treated by means of autonomous differential equations and systems of equations, where examples are developed and other problems and exercises are presented for the reader to develop.

The authors of (Ruiz, et al., 2016) indicate a set of articles that form a collection of several problems that are modeled in different processes, but in general the qualitative and analytical theory of differential equations is used in both autonomous and non-autonomous cases, in both books the problem of epidemic development is addressed.

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The objective of this work is to perform a modeling using ordinary differential equations, the infection process using COVID-19 in such a way that it can respond to the current situation in different countries and regions where the problem of multiple waves is presented; as it happened in Cuba and other countries, a possibility that had already been indicated in (Ruiz, et al., 2020), where in addition it was planted how to reverse this situation.

2. MATHEMATICAL MODEL FORMULATION

The process of infection by means of the SARS-CoV-2 coronavirus until effective measures are not taken has an exponential growth rapidly appearing many infected individuals, leading to many of them death if urgent measures are not taken. It is known that to carry out the study of a model that simulates the process it is necessary to see how the susceptible population will decrease proportionally to their concentration because they can by their immune system pass directly to recovered, and decrease by meeting with infected.

The population recovered decreases in proportion to its concentration and increases in proportion to the concentration of those infected whit the concentration of susceptible. By other hand concentration of the infected population will decrease proportionally to its concentration and will increase proportionally to the product of the infected population whit susceptible population, adding the product between infected and recovered, that is in the case where sgi$_1$ (t-1)>0, otherwise, the variation will be null.

In order to formulate the model using a system of differential equations, the following variables will be introduced:

i_1 is the total concentration of the infected population at time t.
s_1 is the total concentration of the population of susceptible at time t.
e_1 is the total concentration of the exposed population at time t.
r_1 is the total concentration of the recovered population at time t.

Furthermore, the open set will be denoted V_α as,

$$V_\alpha = \{(\bar{i}_1, \bar{s}_1, \bar{e}_1, \bar{r}_1) \in R^3 / a - \alpha < \bar{i}_1 < a + \alpha, b - \alpha < \bar{s}_1 < b + \alpha, c - \alpha < \bar{e}_1 < c + \alpha,$$
$$d - \alpha < \bar{r}_1 < d + \alpha\}$$

Where $\bar{i}_1$, $\bar{s}_1$, $\bar{e}_1$ and $\bar{r}_1$ they represent admissible concentrations of infected, susceptible, exposed and

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recovered populations, as it is assumed that once the pandemic appears, it will not disappear completely.

Here i_1, s_1, e_1 and r_1 are defined as: $i_1 = \cancel{i}_1 - \bar{i}_1$, $s_1 = \cancel{s}_1 - \bar{s}_1$, $e_1 = \cancel{e}_1 - \bar{e}_1$ and $r_1 = \cancel{r}_1 - \bar{r}_1$ so if $i_1 \to 0$, $s_1 \to 0$, $e_1 \to 0$ and $r_1 \to 0$ the following conditions would be met $\cancel{i}_1 \to i_1$, $\cancel{s}_1 \to \bar{s}_1$, $\cancel{e}_1 \to e_1$ and $\cancel{r}_1 \to \bar{r}_1$ that would constitute the main objective of this work. Considering the previous principles, mathematical modeling takes the following form,

$$\begin{cases} i_1' = sg\left(i_1(t-1)\right)[-a_1 i_1 + a_2 s_1 + a_3 e_1 + a_4 r_1 + I_1(i_1, s_1, e_1, r_1)] \\ s_1' = -b_1 s_1 - b_2 i_1 s_1 + S_1(i_1, s_1, e_1, r_1) \\ e_1' = -c_1 e_1 + c_2 i_1 s_1 + E_1(i_1, s_1, e_1, r_1) \\ r_1' = d_1 i_1 - d_2 r_1 + R_1(i_1, s_1, e_1, r_1) \end{cases} \tag{1}$$

The parameters that appear in the system correspond to:
a_1 is the coefficient of decrease of those infected due to their own concentration.
a_2 is the increase coefficient of those infected by the encounter with a susceptible.
a_3 is the growth coefficient of those infected as a function of those exposed.
a_4 is the growth coefficient of the infected as a function of the recovered non-immunized.
b_1 is the coefficient of decrease of the susceptive in function of their own concentration.
b_2 is the coefficient of decrease of the susceptive by the encounter by the encounter with infected.
c_1 is the coefficient of decrease of exposed in function of its own concentration.
c_2 is the coefficient of decrease of exposed by the encounter with infected.
d_1 is the growth coefficient of the recovered depending on the concentration of the infected.
d_2 is the decrease coefficient of the recovered ones due to their own concentration.

3. QUALITATIVE STUDY

If $i_1(t-1) \neq 0$ then, is positive and so $sg\left(i_1(t-1)\right) = 1$, and so system (1) has the form,

$$\begin{cases} i_1' = -a_1 i_1 + a_2 s_1 + a_3 e_1 + a_4 r_1 + I_1(i_1, s_1, e_1, r_1) \\ s_1' = -b_1 s_1 - b_2 i_1 s_1 + S_1(i_1, s_1, e_1, r_1) \\ e_1' = -c_1 e_1 + c_2 i_1 s_1 + E_1(i_1, s_1, e_1, r_1) \\ r_1' = d_1 i_1 - d_2 r_1 + R_1(i_1, s_1, e_1, r_1) \end{cases} \tag{2}$$

With the initial conditions, $i_1(0) = i_{10}$, $s(0) = s_{10}$, $e_1(0) = e_{10}$, $r(0) = r_{10}$.

The characteristic equation corresponding to the matrix of the linear part of this system (2) has the form
$(-b_1 - \lambda)(-c_1 - \lambda)[\lambda^2 + (a_1 + d_2)\lambda + a_1 d_2 - d_1 a_4] = 0$

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Theorem 1: If the condition $a_1 d_2 > d_1 a_4$ then, the null solution of system (2) is satisfied, it is asymptotically stable, and thus the total concentrations of the populations corresponding to infected, susceptible, exposed and recovered converge to the admissible concentrations.

The proof of this theorem is a direct result of the Hurwitz conditions, which guarantees the negativity of the real parts of the roots of the characteristic equation, in correspondence with the method of the first approximation.

Remark 1: The result corresponding to **Theorem 1**, allows to affirm that in this case the infection is controlled, because although the active cases are not eliminated, there is also no epidemic, since the infected ones correspond with those that the country can file.

Remark 2: When $a_1 d_2 = d_1 a_4$ then, we are in the presence of a critical case, and it can be treated in the same way as the treatise in this paper.

If $i_1(t-1) = 0$, then the previous system1 has the form,

$$\begin{cases} i_1' = 0 \\ s_1' = -b_1 s_1 - b_2 i_1 s_1 + S_1(i_1, s_1, e_1, r_1) \\ e_1' = -c_1 e_1 + c_2 i_1 s_1 + E_1(i_1, s_1, e_1, r_1) \\ r_1' = d_1 i_1 - d_2 r_1 + R_1(i_1, s_1, e_1, r_1) \end{cases} \tag{3}$$

with the initial conditions, $i_1(0) = 0$, $s(0) = s_{10}$, $e_1(0) = e_{10}$, $r(0) = r_{10}$

In this case, the characteristic equation corresponding to the matrix of the linear part of this system (3) has the form $\lambda(-c_1 - \lambda)(-b_1 - \lambda)(-d_2 - \lambda) = 0$.

This is a critical case, since the system has a null eigenvalue and the remaining three have a negative real part, therefore it is not possible to apply the first approximation method to determine the stability of the null solution of system 3. In this case, it is necessary to apply the second Lyapunov method once this system has been simplified. By means of a non-degenerate transformation $X = SY$, where $X = (i_1, s_1, e_1, r_1)^t$ and $Y = (i_2, s_2, e_2, r_2)^t$, the system (3) can be transformed into the system,

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$$\begin{cases} i_2' = I_2(i_2, s_2, e_2, r_2) \\ s_2' = \lambda_1 s_2 + S_2(i_2, s_2, e_2, r_2) \\ e_2' = \lambda_2 e_2 + E_2(i_2, s_2, e_2, r_2) \\ r_2' = \lambda_3 r_2 + R_2(i_2, s_2, e_2, r_2) \end{cases} \quad (4)$$

The functions S_2, R_2, E_2 and I_2 admit the following development in series of converging powers in a neighborhood of the origin of coordinates, which have the form,

$S_2(i_2, s_2, e_2, r_2) = \sum_{|p|\geq 2} S_2^{(p)} i_2^{p_1} s_2^{p_2} e_2^{p_3} r_2^{p_4}, \quad |p| = p_1 + p_2 + p_3 + p_4.$

Because it is a critical case, the analytical theory of differential equations will be applied to simplify the system.

Theorem 2: The exchange of variables,

$$\begin{cases} i_2 = i_3 + h_1(i_3) + h^0(i_3, s_3, e_3, r_3) \\ s_2 = s_3 + h_2(i_3) \\ e_2 = e_3 + h_3(i_3) \\ r_2 = r_3 + h_4(i_3) \end{cases} \quad (5)$$

transforms the system (4) into almost normal form,

$$\begin{cases} i_3' = I_3(i_3) \\ s_3' = \lambda_1 s_3 + S_3(i_3, s_3, e_3, r_3) \\ e_3' = \lambda_2 e_3 + E_3(i_3, s_3, e_3, r_3) \\ r_3' = \lambda_3 r_3 + R_3(i_3, s_3, e_3, r_3) \end{cases} \quad (6)$$

Where $h_i, (i = 1,2,3,4)$, h^0, S_3, E_3, R_3 and I_3 admit a similar development S_2, R_2, E_2 and I_2, besides that h^0, S_3, E_3 and R_3 cancel when $\mathrm{s}_3 = \mathrm{e}_3 = \mathrm{r}_3 = 0$.

Proof: Deriving the transformation (5) along the trajectories of the systems (4) and (6) the system of equations is obtained,

$$\begin{cases}(p_2\lambda_1+p_3\lambda_2+p_4\lambda_3)h^0+I_3=I_2-\frac{dh_1}{di_3}I_3-\frac{\partial h^0}{\partial i_3}I_3-\frac{\partial h^0}{\partial s_3}S_3-\frac{\partial h^0}{\partial e_3}E_3-\frac{\partial h^0}{\partial r_3}R_3\\ S_3=S_2-\frac{dh_2}{di_3}I_3\\ E_3=E_2-\frac{dh_3}{di_3}I_3\\ R_3=R_2-\frac{dh_4}{di_3}I_3\end{cases}\qquad(7)$$

To determine the series that intervene in the systems and the transformation, we will separate the coefficients from the powers of degree $p=(p_1,p_2,p_3,p_4)$ in the following two cases:

Case I) Doing $s_3=e_3=r_3=0$ in the system (7), is to say for the vector $p=(p_1,0,0,0)$ the system results,

$$\begin{cases}I_3(i_3)=I_2(i_3+h_1,h_2,h_3,h_4)-\frac{dh_1}{di_3}I_3\\ \lambda_1h_2=S_2(i_3+h_1,h_2,h_3,h_4)-\frac{dh_2}{di_3}I_3\\ \lambda_2h_3=E_2(i_3+h_1,h_2,h_3,h_4)-\frac{dh_3}{di_3}I_3\\ \lambda_3h_4=R_2(i_3+h_1,h_2,h_3,h_4)-\frac{dh_3}{di_3}I_3\end{cases}\qquad(8)$$

The system (8) allows to determine the series coefficients, $h_i(i_3),(i=1,2,3,4)$ and $I_3(i_3)$ where for being the resonant case $h_1=0$, the remaining series are determined in a unique way.

Case II) When $s_3\neq 0$, $e_3\neq 0$ and $r_3\neq 0$, from system (7) it follows that,

$$\begin{cases}(p_2\lambda_1+p_3\lambda_2+p_4\lambda_3)h^0=I_2-\frac{\partial h^0}{\partial i_3}I_3-\frac{\partial h^0}{\partial s_3}R_3-\frac{\partial h^0}{\partial e_3}S_3-\frac{\partial h^0}{\partial r_3}R_3\\ S_3=S_2(i_3+h_1+h^0,s_3+h_2,e_3+h_3,r_3+h_4)\\ E_3=E_2(i_3+h_1+h^0,s_3+h_2,e_3+h_3,r_3+h_4)\\ R_3=R_2(i_3+h_1+h^0,s_3+h_2,e_3+h_3,r_3+h_4)\end{cases}\qquad(9)$$

Since the series of system (4) are known expressions, system (9) allows us to calculate the series h^0, S_3, E_3 and R_3. This proves the existence of variable exchange.

In system (6), function $I_3(i_3)$ admits the following development in power series:
$I_3(i_3)=\alpha i_3^n+\ldots$

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Where α is the first non-zero coefficient of $I_3(i_3)$ and n is the corresponding power.

Theorem 3: If $\alpha < 0$ and n is odd, so the trajectories of the system (8) are asymptotically stable, otherwise they are unstable.

Proof: Consider the Lyapunov function defined positive,

$$V(i_3, s_3, e_3, r_3) = \frac{1}{2}(i_3^2 + s_3^2 + e_3^2 + r_3^2)$$

The derivative along the trajectories of the system (8) has the following expression,

$$V'(i_3, s_3, e_3, r_3) = \alpha i_3^{n+1} + \lambda_1 s_3^2 + \lambda_2 e_3^2 + \lambda_3 r_3^2 + R(i_3, s_3, e_3, r_3)$$

Because in R the powers of degrees greater than the second are grouped with respect to s_3, e_3 and r_3 and higher grade $n+1$ respect to i_3 in the expression of the derivative of V, this allows to affirm that the equilibrium position is asymptotically stable, thus the populations of infected, susceptible, exposed and recovered converge to the admissible conditions.

Remark 3: The **Theorem 3** of the necessary and sufficient conditions for the convergence of the total concentrations of the populations to the admissible concentrations.

Remark 4: The combination of problems (2) and (3) allows us to perceive the appearance of multiple waves as indicated in the objective of the work.

Remark 5: By solving the problem (2), the behavior of the pandemic can be predicted at a specific time.

4. COMPUTATIONAL PROCEDURE

The process from a computational point of view can be governed by an algorithm, which can be programmed from a computational point of view; this process is initially described by the trajectories of the problem (1)-(2); once the data decrease, the solution path of the same problem in correspondence with the infection is described; when the infection disappears, the process is governed by the trajectories of the problem (3)-(4); and if new cases appear, a new wave will appear, which is possible even without the infection disappearing completely; when the infection is decreasing and it starts growing again, then problem (1)-(2) will be used again, with the initial condition of the value at which the infection starts to grow, thus appearing a new wave without completely disappearing the previous one . This process can be repeated a certain number of times, with multiple waves of infection appearing.

Example: Let the following system simulate the process of coronavirus infection in a given population.

$$\begin{cases} i_1' = sgi_1(t-1)(-10^{-2}i_1 + 10^{-1}e_1) \\ s_1' = -10^{-7}i_1 s_1 \\ e_1' = -10^{-3}e_1 + 10^{-40}i_1 s_1 \\ r_1' = 10^{-20}i_1 - 10^{-3}r_1 \end{cases}$$

With the initial conditions,

$i_2(0) = i_{20}, s_2(0) = s_{20}, e_2(0) = e_{20}, r_2(0) = r_{20}$

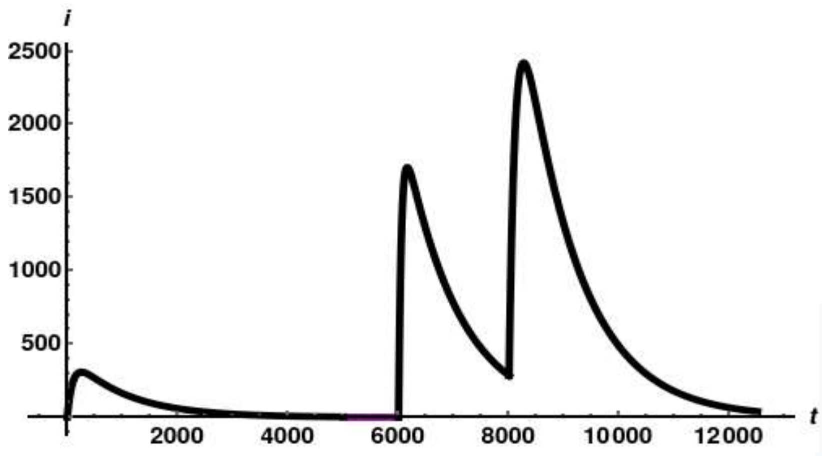

Fig. 1: Graph of infected people over time.

The example shows in practice what is indicated in theory; because here the reproduction of multiple waves was observed once the corresponding graph was made, this corresponds to the development of the problems mentioned above, where the appearance of the waves caused by the pandemic in different countries of the world was confirmed.

Remark 6: The graph corresponding to the example indicated allows to corroborate in practice the result treated in theory, because as seen in different countries and regions of the world, the pandemic has presented itself with multiple waves. This was done following the procedure indicated according to the computational algorithm.

Remark 7: For the appearance of a new hi, it is not necessary for the infected population to disappear completely; in this process, there may be a continuous decrease in cases and from a moment on, a regrowth may appear, in which case $i_2(0) \neq 0$, this corresponds to a new hello that may also appear on the graph.

5. CONCLUSION

Due to the danger to the life of the man, it is of paramount importance to study the characteristics of the SARS-CoV-2 coronavirus, the ways of transition and the methods of combating the disease, which would allow a more effective treatment to patients, this is more evident today with the appearance of multiple waves, which represents a renewal of the disease.

Historically there have been diseases that, due to their spread, have become epidemics, but never with the danger of the SARS-CoV-2 coronavirus and worse with the appearance of new strains linked to multiple waves.

If $a_1 d_2 > d_1 a_4$ then, the total concentrations of the populations corresponding to susceptible, recovered and infected populations are satisfied converge to the admissible concentrations.

When $a_1 d_2 = d_1 a_4$ then, we are in the presence of a critical case and it can be treated in the same way as the treatise in this paper.

If $sg\big(i_1(t-1)\big) = 0$ and $a_1 d_2 > d_1 a_4$ then, you have a critical case for which it is necessary to use the qualitative theory of differential equations to reach conclusions regarding the studied process.

Theorem 2 gives the technique to follow to simplify the system corresponding to the model given by the infection process by means of SARS-CoV-2 coronavirus, in the case where $sg\big(i_1(t-1)\big) = 0$.

If $\alpha < 0$ and n it is unique, so in the critical case, the total concentrations of the infected, recovered and susceptible population converge to the admissible concentrations and thus the infection process would be controlled.

The graph corresponding to the example indicated allows to corroborate in practice the result treated in theory, because as seen in different countries and regions of the world, the pandemic has been presented with multiple waves.

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